II. REMARKS

Reconsideration of the present application in view of the following remarks is respectfully requested.

Claims 1-2 and 5-17 are currently pending. Claims 1 and 2 have been amended and claims 3 and 4 have been canceled without prejudice. Support for the amendments to claims 1 and 2 can be found in the original specification as filed, e.g., the paragraph bridging pages 2 and 3.

A. REJECTION UNDER 35 U.S.C. § 102(b)

Claims 1, 2, 4-14 and 16 were rejected under 35 U.S.C. §102(b), as being anticipated by WO 90/04965 to Lee et al. (hereafter "WO '965"). The Office Action stated that WO '965 "discloses a transdermal preparation and device comprising an opioid analgesic and an opioid antagonist. The antagonist negates the analgesic properties of the opioid if the dosage form is delivered via bolus injection or oral delivery. The antagonist is not permeable through the skin in the transdermal presentation, and is incorporated with the same vehicle of the opioid analgesic."

In response, Applicants respectfully direct the Office to independent claims 1 and 2, which recite, in part, the distressing substance "selected from the group consisting of emetics, nauseants, flavouring substances, bitter substances, ergolides, quaternary ammonium compounds, atropine or salts thereof, and mixtures thereof." Applicants respectfully contend that WO '965 does not teach or suggest an opioid transdermal delivery device comprising a distressing substance selected from the instantly claimed group consisting of emetics, nauseants, flavouring substances, bitter substances, ergolides, quaternary ammonium compounds, atropine or salts thereof, and mixtures thereof. Therefore, Applicants respectfully contend that WO' 965 does not anticipate claims 1, 2, 4-14 and 16, and request withdrawal of the 35 U.S.C. § 102(b) rejection of the claims.

B. Rejection under 35 U.S.C. § 103

Claims 3, 15 and 17 were rejected under 35 U.S.C. § 103(a), as being unpatentable over the combined disclosures of WO '965 and U.S. Patent No. 5,051,426 to Parnell (hereafter the '426). The Office Action states that '965 lacks "disclosure of ergolide compounds as possible antagonists or distressing compounds." The Office Action further states that '426 "discloses methods and compositions for the treatment of drug dependent withdrawal symptoms. The composition delivers a CNS stimulant, which can be opioid analgesics such as codeine and morphine, in association with a serotonin antagonist such as ergolide. The antagonist inhibits the action of serotonin, essentially removing the euphoric properties of the composition." The Examiner concludes that "a skilled artisan would have been motivated to combine the antagonists of '462 into the formulation of WO '965.

This rejection is respectfully traversed. Applicants respectfully submit that the Office Action mischaracterizes '426 (for example see page 4, lines 5-7) by contending that it teaches "a CNS stimulant, which can be opioid analgesics such as codeine and morphine, in association with a serotonin antagonist such as ergolide." . The CNS stimulant disclosed in '426 is preferably a xanthine compound such as caffeine. The CNS stimulant (not an opioid) is administered in association with the serotonin antagonist as replacement therapy for a drug of abuse (e.g., an opioid) to effect withdrawal. '426 describes the CNS stimulant/serotonin antagonist combination as replacement therapy for a drug such as an opioid and therefore actually teaches away from a dosage form containing both an opioid and a serotonin antagonist. Accordingly, Applicants respectfully contend that '426 does not teach an opioid in association with a serotonin antagonist as alleged in the Office Action.

Applicants further contend that when the serotonin antagonist of '426 is included in a transdermal delivery device, the serotonin antagonist is in a form to actually be administered through the skin when the composition is applied transdermally. In support of this statement, Applicants direct the Examiner to the column 7, lines 3-19 of '426 which read as follows:

> The compounds of the invention may also be delivered through the body surface, i.e., transdermally or transmucosally. By "transdermal" as used herein is meant passage into and **through the skin** to achieve effective therapeutic blood levels.
> (Emphasis added)

In contrast, the antagonist in the instantly claimed composition is in a form which is non-permeant through human skin and is present to distress an abuser when the transdermal system is used inappropriately, such as when ingested orally, or when administered as a parenteral bolus injection together with the opioid analgesic .

Applicants respectfully submit that '426 does provide one of ordinary skill in the art to the motivation to modify the formulation of WO '965 to arrive at a transdermal system with a distressing substance which is non-permeant through the skin upon application, because '426 is directed to administering agents which are intended to be absorbed through the skin upon application.

For at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejection of claims 3, 15, and 17.

IV. CONCLUSION

In view of the foregoing, Applicants believe that the above-referenced rejections have been obviated and respectfully request that all rejections be withdrawn. Applicants believe that all claims are now in condition for allowance. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution of the present application. An early and favorable action is earnestly solicited.

Respectfully submitted,
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